

## **IN THE CLAIMS**

Cancel original claims 1-42 and add the following new claims 43-52.

1. – 42. (canceled)

43. (New) A method for producing a protein free from infectious prion contamination, comprising:

- a) ablating an endogenous PrP gene in a mammalian somatic host cells;
  - b) operatively inserting a DNA sequence into said host cells which sequence encodes a protein; and
  - c) isolating the protein from said host cells;
- wherein the isolated protein is in a composition which is characterized by an inability to transmit a prion-mediated pathology to a subject of the same species as the host cells.

44. (New) The method of claim 43, wherein the protein is a human protein.

45. (New) The method of claim 43, wherein both alleles of the endogenous PrP gene are ablated.

46. (New) A method for producing a therapeutic protein composition free from infectious prion contamination, comprising:

- a) ablating an endogenous PrP gene in a host mammalian cell;
  - b) introducing exogenous PrP sequences from a species genetically diverse from said host cell into said host cell;
  - c) expressing said exogenous PrP sequences;
  - d) operatively inserting a DNA sequence into said host cell which sequence encodes a protein; and
  - e) isolating a composition comprising the protein from said host cell;
- wherein the expression of the exogenous PrP sequences allows necessary expression of PrP and wherein the isolated composition cannot transmit a prion-mediated pathology to a subject of the same species as the host cell.

47. (New) The method of claim 46, wherein the exogenous PrP gene is operatively fused to an inducible promoter.

47. (New) The method of claim 46, wherein the exogenous PrP gene is operatively fused to an inducible promoter.

48. (New) The method of claim 46, wherein the protein is human.

49. (New) The method of claim 46, wherein both alleles of the endogenous PrP gene are ablated.

50. (New) A method for producing a therapeutic protein composition free from infectious prion contamination, comprising:

- a) ablating the endogenous PrP gene in a somatic host cell;
- b) introducing exogenous PrP sequences from a genetically similar species, said exogenous sequences operably linked to an inducible promoter;
- c) suppressing expression of the exogenous PrP sequences;
- d) producing a therapeutic composition comprising a protein in said host cell; and
- e) isolating the therapeutic composition from said host cell;

wherein the isolated therapeutic protein composition produced during suppression of PrP expression cannot transmit a prion-mediated pathology to a subject of the same species as the host cell.

51. (New) The method of claim 50, wherein the protein is human.

52. (New) The method of claim 50 wherein both alleles of the endogenous PrP gene are ablated.